

Original Research Article

The association between blood glucose level and cognitive dysfunction among acute traumatic brain injury in Manado, Indonesia

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ABSTRACT

Background: Traumatic brain injury (TBI) is a public health challenge. TBI contributes to chronic physical impairment and also disrupt mental and personality aspects. Cognitive dysfunction is influenced by multiple factors, including blood glucose level. The objective of the study was to analyze the association between blood glucose level and cognitive dysfunction among TBI patients.

Methods: A hospital-based observational study was conducted with cross-sectional design for six months period. Population of research were all of TBI patients treated at the emergency unit. Eligible sample were obtained with total sampling technique. Dysglycemia was defined as random blood glucose level outside the range of 80-200mg/dl; cognitive dysfunction was defined as MMSE score <26. Statistical analysis with SPSS version 17.0 was employed. Chi square test and odd ratio were executed, p value <0,05 were regarded as significant level.

Results: Majority of the 124 patients was male (75.8%), in 21-30 age group (20.7%), mostly due to RTA, specifically from motorcycle-related accident. Most of the motorcyclist (56,5%) were not using helmet. Unconsciousness was in 65.8% sample. Seizure was found in 3.9% of total patients; almost half of patients had history of headache (40.8%). Vomit was found in 30.3% of patients. Vertigo or dizziness post-trauma was in 3.9% patients; almost one third of patients had history of alcohol consumption (30.3%). Majority (65.8%) were in GCS 13-15. Proportion of dysglycemia and cognitive dysfunction were 4.8% and 14.5% consecutively. Odd ratio analysis revealed that dysglycemic group have 3 times higher risk to develop cognitive dysfunction, but the association was statistically not significant.

Conclusions: The association between random blood glucose level and cognitive dysfunction among acute traumatic brain injury was statistically not significant.

Keywords: Blood glucose, Cognitive, Dysglycemia, Head trauma, Traumatic brain injury

INTRODUCTION

Traumatic brain injury (TBI) is becoming one of the public health challenges worldwide. It is the number one killer among young people and most of the cases were happened in poor and developing countries. TBI is the important cause of physical disabilities in many countries especially in productive people. Recent epidemiological

trend of TBI have shown that the cases occur in every age group, sex and nations.¹⁻⁵

In Indonesia, the transition of demographic and epidemiology were affected by modernization in transportation modes. According to Ministry of Health (MOH), in 2013 almost half (40,6%) of all traumatic cases were due to traffic accidents. In Manado, among the victims from road traffic accident (RTI), majority of

death (77,7%) were due to TBI, mostly in 20-40 age group.^{6,7}

TBI contribute to chronic physical impairment and also disrupt the mental and personality aspects of the patients. Cognitive dysfunction in young people were mostly related to TBI. Attention and concentration disorder, memory and language problem, visuo-spatial limitation and executive dysfunction are the domain of cognitive function which could be hampered by TBI. In the majority of the cases, the dysfunction was initially undetectable during acute phase. Patient and families recognized and reported the problem after the patients back to the daily activities. Problem in finding words, concentration, academic and work performance are common. These problem leads to social limitation. Problem in social interaction due to cognitive dysfunction could lead to productivity issues among young people and their freedom and personal interaction.⁸⁻¹⁰

Cognitive dysfunction was influenced by many contributing factors. One of the most important factors during acute phase of TBI is blood glucose level. Glucose metabolism during acute critical illness were highly correlated with the outcome. Most of the final outcome in relation to TBI were focused on physical issues such as complication and death. There is lack of data regarding the association between blood glucose level in admission and cognitive dysfunction among TBI patients, especially in acute phase.^{11,12} Therefore, the objective of the study was to analyze the association between random blood glucose level and cognitive dysfunction among TBI patients treated in emergency room.

METHODS

This was an observational study with cross-sectional design for six months study period at Prof. dr. R. D. Kandou Hospital Manado. Population of research were all of the TBI patients treated at the emergency unit. Sample were obtained with total sampling technique. Eligibility criteria were consisted of inclusion and exclusion criteria. Inclusion criteria were mild and moderate TBI, willingness to participate in study, in the age between 15-60 years old, onset less than 24 hours and had family and/or caregiver at the time of data collection. Exclusion criteria were the history of psychiatric condition, dementia, epilepsy, diabetes, hypertension, underwent corticosteroid treatment, chronic alcoholism, language problems and attention disorders. Patient with consciousness recovery more than 24 hours were also excluded.

During study period, there were 124 TBI patients were analyzed. The definition of TBI on the study was history of trauma to head by external mechanical force. The study operational definition for dysglycemia was random blood glucose level less than 80 mmHg or above 200mmHg. Cognitive dysfunction was measured with Mini Mental Status State Examination (MMSE) less than

26. Type of head injury was mostly categorized based on Glasgow Coma Scale score after resuscitation.

Traumatic patient was primarily assessed and managed adequately according to trauma protocol in the hospital before obtaining history and physical examination in secondary survey phase. Patients and their families/caregivers were informed about the objective of the study before consent was obtained. Primary data were collected with the interview with patient and/or caregivers. Patient were asked to answer structured questionnaire. Ethic permission were requested to the hospital Ethic Committee.

Authors presented all descriptive data in number and percentage. Statistical analysis with SPSS version 17.0 was employed. Chi square test and odd ratio were executed during statistical analysis, with p value <0.05 were regarded as significant level.

RESULTS

During study period there were 124 patients admitted to the ER with acute head trauma. Majority of the patients was male (75.8%), most of them was in 21-30 age group (20.7%) and 31-40 age group (13.0%). History of road traffic accident/RTA was the majority type of head trauma, specifically from motorcycle-related accident. Among patients with motorcycle-related traffic injury, most of them were not using helmet at the moment of accident (56.5%) (Table 1).

Table 1: Distribution of demographic characteristics.

Characteristics	N (=124)	%
Sex		
Male	94	75.8
Female	30	24.2
Age group (year)		
Below 21	6	4.8
21-30	40	20.7
31-40	25	13.0
41-50	21	10.9
51-60	10	5.2
Above 60	22	11.4
Type of head trauma		
No information	3	2.4
Fall	17	13.7
RTA motorcycle (helmet +)	19	15.3
RTA motorcycle (helmet -)	70	56.5
RTA car accident	15	12.1

In the present study, more than half of the TBI patients were admitted with unconsciousness as chief complaint (65.8%). Seizure after head trauma was found in 5 patients (3.9%). Almost half of the patients with history of headache (40.8%). Vomit was found in 30.3% of patients. Vertigo or dizziness post-trauma was found in

3.9% patients. Almost one third of the patients were admitted to hospital with the history of alcohol consumption (30.3%). Glasgow Coma Scale (GCS) examination revealed that majority of the cases (65.8%) were in GCS 13-15. As the main research variable, dysglycemia was detected in 4.8% of TBI cases and cognitive dysfunction was 14.5% (Table 2).

Table 2: Distribution of clinical characteristics.

Characteristics	N (=124)	%
Unconsciousness		
Yes	82	65.8
No	42	34.2
Seizure		
Yes	5	3.9
No	119	96.1
Headache		
Yes	51	40.8
No	73	59.2
Vomit		
Yes	38	30.3
No	86	69.7
Vertigo		
Yes	5	3.9
No	119	96.1
Alcohol consumption		
Yes	38	30.3
No	86	69.7
GCS		
3-8	7	5.3
9-12	36	28.9
13-15	81	65.8
Dysglycemia		
Yes	6	4.8
No	118	95.2
Cognitive dysfunction		
Yes	18	14.5
No	106	85.5

In the present study, there were 2 patients (33.3%) with both dysglycemia and cognitive dysfunction. Among non dysglycemia group, there were 13.6% with cognitive dysfunction. Odd ratio analysis revealed that dysglycemic group have 3 times higher risk to develop cognitive dysfunction than non-dysglycemic group. Statistical

analysis showed that the association was not significant ($p>0.05$) (Table 3).

DISCUSSION

The present study showed that the ratio of male to female were 3:1 which was similar to almost majority of study about TBI. In Nigeria, Adogu reported the ratio was 3.4-3.5:1 and in India Narwade reported the ratio of 6.1:1 in their 3 year study about clinical profile and management of TBI. The male preponderance was higher due to the higher risk of male to consume alcohol while driving, lack of obedience to traffic warning signs and their tendency to be in rush.^{2,13}

In this study most of the victim were also in young people in their very productive age group, majority of case were in 21-30 age group. This study was similar to the incidence of head trauma in Nigeria where the peak incidence was found in 20-30 age group, and India also in the same group of age. In USA, the highest incidence was found in 15-19 age group as cited by Adogu. According to Adogu regulatory and policy in driving licence might influence this different result.^{2,13,14}

Road traffic accident is the majority source of head trauma in this study. Both motorcycle and car user were the biggest group of patients. Among motorcyclist, more than half were not using helmet at the time of accident. This result is similar to what was reported by Djaja in 2016. According to Djaja during 5 years (2010-2014) most of traffic accidents in Indonesia were from motorcycle. There are several factors that contributes to the situation such as disobedience to traffic signs, careless in driving and breaking the speed limit. In several nations in ASEAN region, motorcycle is increasing in popularity. The number of motorcycle in Indonesia, Thailand and Cambodia is the biggest in the region. This is because remarkable economic growth, big proportion of young people and improvement in highway condition.¹⁵

In the present study, more than half of the TBI patients were admitted with unconsciousness as chief complaint. However, GCS score were commonly found in the range of 13-15. It means, majority of patients in this study were in mild degree of unconsciousness.

Table 3: Distribution of cognitive dysfunction according to dysglycemia status.

Dysglycemia	Cognitive dysfunction				Total		OR (95% CI)	p-value*
	Yes	No			N	%		
	N	%	N	%	N	%		
Yes	2	33.3	4	66.7	6	100	3.18	0.180
No	16	13.6	102	86.4	118	100	0.53 - 18.85	
Total	18	14.5	106	85.5	124	100		

*chi square test

Patients with mild decrease in consciousness would probably be in better outcome. Paydar conducted a study to evaluate relationship between GCS and outcome of TBI patients. They reported that the percentage of increase GCS in the first week were more than half of total patients (62.2%). On their study, GCS 6-8 was common in the first day from onset (43.2%), but the proportion of GCS >8 were more than half of patients in sixth day after onset (60.8%). Patient in deep coma would be in worse outcome. Narwade reported that although the number of patient with deep coma is relatively lower than mild unconsciousness, but the proportion of death is extremely higher in patients with coma.^{3,13}

Several clinical manifestations were need to be considered. The relatively small proportion of seizure in the present study was related to data collection period. Post-traumatic seizure was divided in early- and late-seizure. Early post-traumatic seizure is defined as seizure occurred within 1 week after the onset. Its incidence is about 4-25%. Seizure that occurred more than 1 week after trauma were classified as late seizure, with incidence of 9-42%.¹⁶ In this study, the prevalence of post-traumatic headache was prominent. Almost half of the patients with history of headache. Vomit was found in almost one-third of patients. Vertigo or dizziness post-trauma were found in relatively small proportion. The history of alcohol consumption was obtained in one-third of the patients. The result is lower than other publication. In Narwade's study, they reported that the proportion of patients with history of alcohol consumption were 62.4%. According to Narwade, alcohol consumption might be one of the major contributor for the increasing prevalence of RTI in rural India.¹³

In the present study dysglycemia was detected in 4.8% of all TBI cases. Both hyperglycemia and hypoglycemia were reported negatively contribute to patients' outcome. The proportion of poor outcome was reported higher in elevated blood glucose level. In Iran, hyperglycemia status on admission negatively influence the death proportion. In Malaysia, there were different of blood glucose level in different category of TBI. Patients with severe TBI were in higher risk to develop hyperglycemia. However, hypoglycemia also is important in determining patients' outcome. According to Chara, central nervous system has limited tolerance to low glucose level because it will activate contra regulatory mechanisms. During this mechanism, there will be elevated of cerebral blood flow, depletion of glucose, activation of hormonal responses and releasing of glucagon hormones. The mechanism contributes to the activation of glutamate responses and apoptotic pathways.^{11,17,18}

In this study, we detected cognitive dysfunction in 14.5% patients. Pertiwi conducted a research on cognitive disorders after TBI also found significant different of cognitive score than control group. According to Pertiwi, TBI disrupt the functional of brain especially in relation

to neurobehavioral function such as thinking, awareness, emotion and personality. Neuropsychiatric approach in every patient of TBI is recommended as standard protocol.¹⁹

It seems that regardless of the blood glucose level, cognitive function was mainly disrupted by several risk factors during primary and secondary injuries. The present study revealed that the proportion of cognitive dysfunction in TBI patient with abnormal random blood glucose level were relatively high. Similar situation was also found among patients with normal random blood glucose level on admission, one third of them were categorized as cognitive dysfunction. Eakins reported that hyperglycemia is commonly found in acute trauma setting.²⁰ Hyperglycemia is a hyper-metabolism response to acute stress and could be regarded as one of the main characteristics of acute trauma. This condition impairs the outcome of traumatic cases, especially among TBI patients in critical condition. However, in this study we found that although the likelihood of TBI patients with dysglycemia to develop cognitive dysfunction is slightly higher that without dysglycemia, but the association was not statistically significant.

Therefore, the result of the current study was failing to detect the relationship between glucose metabolism in acute phase and cognitive function among TBI patients. In addition to methodological issues, one possible explanation is because there is conflicting result whether plasma blood glucose level was positively correlated with brain glucose level. Some study showed that positive correlation is confirmed between glucose level in plasma and the brain, but other study reported that the relationship was only positive in non-injured hemisphere.^{12,21}

There are several limitations of the present study: The period of data collection was relatively short, resource population was limited to hospital emergency room, data on fasting blood glucose was not obtained, data about variation of blood glucose was not available and severe TBI cases were not included in analysis. Therefore, the result could not be generalized in different setting.

CONCLUSION

In the emergency room, the association between random blood glucose level and cognitive dysfunction among acute traumatic brain injury was statistically not significant. Further population-based longitudinal study with larger sample is recommended. We also suggest studying the variation of blood glucose during acute treatment of TBI and how this variation influence the outcome. Furthermore, qualitative study about cognitive function and quality of life among TBI patients with dysglycemia were encouraged.

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